REMARKS

The Examiner is thanked for the thorough examination of the application. No new matter is believed to be added to the application by this Amendment.

Status Of The Claims

Claims 1, 3 and 5-15 are pending in the application. Claim 2 and withdrawn claim 4 are canceled by this Amendment. Claim 1 has been amended to incorporate subject matter from claim. Claims 5-15 also set forth subject matter from canceled claim 2.

Rejection Under 35 U.S.C. §103(a) Over Tsuchida I and Tsuchida II

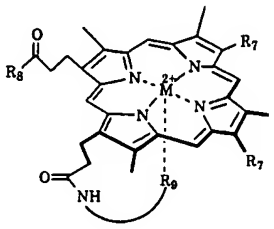
Claims 1-3 have been rejected under 35 U.S.C. §103(a) as being obvious over the combination of Tsuchida I (Tsuchida et al., Bioconjugate Chem., 1999, 10, 797-802) in view of Tsuchida II (Tsuchida et al., Bioconjugate Chem., 2000, 11, 46-50). Applicants traverse.

The Present Invention And Its Advantages

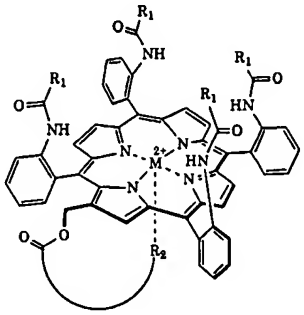
The present invention provides an oxygen infusion for increasing the oxygen concentration in tumor tissues in living bodies and, more particularly, a highly-safe oxygen infusion for effectively increasing oxygen partial pressures in a hypoxic region of the tumor tissues by administering it to a site near tumor tissues of human bodies.

According to the present invention, the above object is achieved by providing an oxygen infusion formed from a dispersion liquid of one or more albumin clathrate compounds dispersed in a physiologically permissible aqueous media, the albumin clathrate compounds including a porphyrin metal complex represented by the general formula (I) or porphyrin metal complexes respectively expressed by the general formulas (I) and (II).

General formula (II)



General formula (I)



The porphyrin metal complex- clathrate albumin compound of the present invention makes it possible to effectively increase the oxygen partial pressure in the tumor tissues. In fact, the oxygen partial pressure is increased up to 2.5 time of the primary oxygen partial pressure (1.4±0.2 Torr) by administration of the oxygen infusion product of the present invention, as demonstrated by Example 1 in the specification. This demonstrates a truly unexpected result over the conventional art.

Distinctions Of The Invention Over Tsuchida I and Tsuchida II

Tsuchida I pertains to 2-[8-{N-(2-methylimidazolyl)}octanoyloxymethyl]-5, 10, 15, 20-tetrakis-(o-(pivalamido) phenylporphyrinatoironi(II)s (FePs) that were incorporated into hydrophobic cavities of recombinant human serum albumin (rHSA), providing a totally synthetic O_2-carrying hemoprotein (rHSA-FeP) and teaches that the O_2-binding affinity and O_2-association

and dissociation rate constants of resultant rHSA-FeP satisfy the initial clinical requirements for O_2 infusion as a red cell substitute (see Abstract of Tsuchida I).

However, Tsuchida I fails to teach or suggest the effects of the porphyrin metal complex -clathrate albumin compound on the oxygen partial pressure in the tumor tissues. That is, Tsuchida I fails to teach or suggest an "oxygen infusion for increasing an oxygen concentration in tumor tissues in living bodies," such as is set forth in claim 1 of the present invention. Therefore, Tsuchida I fails to be usable as the basis of an assertion of obviousness.

On the other hand, Tsuchida II discusses that human serum albumin (HSA) incorporating synthetic hemes, the tetrakis-(o-(pivalamido) phenylporphyrinatoiron(II) derivative (FeP), is an artificial hemoprotein (HSA-FeP) which is able to reversibly bind and release dioxygen under physical conditions like hemoglobin and myoglobin (see abstract of Tsuchida II). Tsuchida II teaches from the evaluation of physiological responses to exchange transfusion with HSA-FeP solution into rats after hemodilution and hemorrhage, that the MAP and blood flow after 70% exchange with HSA and the further 40% bleeding of blood was recovered by injection of HSA-FeP.

However, Tsuchida II fails to teach or suggest the effects of the porphyrin metal complex- clathrate albumin compound on the oxygen partial pressure in the tumor tissues. Tsuchida II thus fails to address the deficiencies of Tsuchida I in teaching or suggesting a claimed embodiment of the present invention.

In contrast, the paragraph bridging pages 4-5 of the specification discusses that cancer cells are in a hypoxic condition, and the presence of the hypoxic cells is one of the reasons that

malignant tumors have resistance to radiotherapy or chemotherapy. Thus, the behaviors of porphyrin metal complex in normal cells differ from that of porphyrin metal complex in cancer cells.

Although attempts to improve anticancer properties and radio sensitivity by increasing the oxygen concentration of the tumor tissue in low-oxygen conditions have been made, there remains a significant problem to be solved, as is discussed in the paragraph bridging pages 6-7 of the specification.

According to the present invention, this problem is solved by use of a porphyrin metal complex-albumin clathrate compound which has a particle size smaller than that of red cells and is able to find a path through irregular blood vessels in the tumor tissue easily, as compared with red blood cells, which in turn makes it possible to effectively increase the oxygen partial pressure in the tumor tissues. Such an effect of the present invention is never expected from the cited references, and thus the present invention is never obvious from the cited references, considered alone or in combination.

As a result, the combination of Tsuchida I and Tsuchida II would fail to motivate one of ordinary skill in the art to produce claim 1 of the present invention. A *prima facie* case of obviousness has thus not been made. Claims depending upon claim 1 are patentable for at least the above reasons. Also, the present invention shows unexpected results over the cited references, as has been discussed above.

This rejection is overcome and withdrawal thereof is respectfully requested.

Information Disclosure Statements

The Examiner is thanked for considering the Information Disclosure Statements filed December 3, 2004 and March 7, 2005 and for making the initialed PTO-449 and PTO-SB/08 forms of record in the application in the Office Action mailed February 1, 2006.

Foreign Priority

The Examiner has acknowledged foreign priority in the Office Action mailed February 1, 2006.

The Drawings

The Examiner is respectfully requested to indicate whether the drawing figures are acceptable in the next official action.

Conclusion

The Examiner's rejection has been overcome, obviated or rendered moot. No issues remain. The Examiner is accordingly respectfully requested to place the application in condition for allowance and to issue a Notice of Allowability

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Robert E. Goozner, Ph.D. (Reg. No. 42,593) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petitions for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of $120.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: June 1, 2006

Respectfully submitted,

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